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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/813,444	03/20/2001	Brent Iverson	MXGN:005USC2	3269

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EXAMINER	
DO, PENSEE T	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 10/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/813,444	IVERSON ET AL.	
	Examiner	Art Unit	
	Pensee T. Do	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-12,15-26 and 46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6-8,11,15-21,25,26 and 46* is/are rejected.

7)☒ Claim(s) *9, 10, 12, 22-24* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

Amendment Entry & Claims Status

The amendment after final filed on May 2, 2006 has been acknowledged and entered.

Claims 13, 6-12, 15-26 and 46 are pending.

Withdrawn Rejection(s)

Rejection under 102 by Slamon is withdrawn herein because Slamon fails to teach a library of vectors.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6, 7, 16 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6 and 16 are the same. Either claim should be canceled.

Claims 7 and 17 are the same. Either claim should be canceled.

Claim 26 seems to recite a misspelled word "band". Please correct.

Claim Rejections - 35 USC § 102

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-3, 6-8, 16-21 and 46 are rejected under 35 U.S.C. 102(e) as being anticipated by Higuchi et al. (US 6,214,613).

Higuchi teaches a method for selecting a eukaryotic host cell that expresses a desired antibody or antibody fragments from a plurality of host cells expressing candidate antibodies or antibody fragments, the method comprising: obtaining a vector that has different sequences, one sequence coding is for H-chain variable regions of antibodies and another sequence coding for L-chain variable regions of antibodies. The vector provides cell surface expression of candidate antibodies or fragments. Selecting a host cell that expresses the desired antibody by contacting said antibody/fragment-expressing cells with a selected antigen; and identifying the host cells that bind to the selected antigen . The antigen is labeled with fluorescent (see col. 3, line 10-col. 4, line 21). Antibodies expressed on the membrane of the host cells are secretory type and membrane bound type. The constant region of eh antibodies was made in secretory type for possible expression of the antibodies, and the transmembrane domain of the

membrane protein other than antibody is linked to carboxyl terminus of H-chain and/or L-chain of the antibodies for expressing the antibodies on the cell membrane. In case that any one of a nucleotide sequence of AKL and AKH is integrated in the vector, the chain, which is not integrated therein is previously incorporated in the host cells, or should be incorporated in the host cells by co-transduction of the other vector containing the chain. (see col. 5, lines 35-55). Thus, Higuchi teaches a plurality of vectors being incorporated into the host cells. The vectors express different types of antibodies such as secretory antibodies and membrane bound antibodies. (see col. 5, lines 35-45). Regarding claims 6 or 16, Higuchi teaches a method of selecting a host cell that expresses a desired antibody comprises the steps of contacting the antibody/fragment expressing cells with a selected antigen; and identifying the host cell that binds to said selected antigen. (see col. 7, lines 35-48). For claims 7 and 8 or 17 and 18, the antigen is labeled with fluorescent in Higuchi. (see col. 5, lines 47-48). Regarding claim 19, Higuchi teaches the method of selecting antibody expressing cells by contacting the cells with labeled antigens to allow specific antigen-antibody binding and removing non-binding cells by washing; and detecting the labels of the bound cells. (see col. 12, lines 35-45). Regarding claims 20 and 21, automated cell sorting is by flow cytometry. (see col. 12, lines 46-50). Regarding claim 46, Higuchi teaches that the eukaryotic cells are mammalian cells or human cells. (see col. 5, line 27; example 7-human cells). Regarding claims 2-3, since Higuchi teaches that host cells are eukaryotic cells, it is inherent that eukaryotic cells encompass yeast, mold, algae or insect cells.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 11, 15 and 25-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Higuchi in view of Slamon (US 4,918,162).

Higuchi has been discussed above.

However, Higuchi fails to teach a method of obtaining a vector library by administering to an animal an antigen; obtaining from the animal a plurality of distinct DNA segments that encode distinct antibodies or fragments; and incorporating said plurality of DNA segments into a plurality of vectors; the vectors expressing antibodies on the outer membrane surface of a host cell; and a using magnetic bead linked to the antigen; subjecting the expressed antibody to cleavage to release the antibody from the surface of the outer membrane.

Slamon teaches methods for identifying and monitoring human cancers. The methods rely on the detection of N-myc protein in a biological specimen, usually a cell sample such as tissue sample or sputum sample. Presence of the N-myc protein in the biological specimen may be diagnostic and/or prognostic of the cancer. Polypeptides and antibodies are used for detecting the N-myc proteins, where the polypeptides are associated with immunogenic sites on the protein. The polypeptides may be natural or synthetic. Such polypeptides include the N-myc protein in substantially pure form as well as fragments thereof. Monoclonal or polyclonal antibodies against the polypeptides

are prepared by conventional techniques. Six polypeptides capable of eliciting antibodies useful in the present method have been identified. The method of synthesizing the polypeptides involves the expression in cultured cells of recombinant DNA molecules encoding a desired portion of the N-myc gene. Suitable cDNA and genomic libraries may be obtained from human cell lines known to contain the N-myc gene. (see col. 1, line 65-col. 2, line 48; col. 4, lines 36-49). The natural or synthetic DNA fragments coding for a desired N-myc fragment will be incorporated in DNA constructs capable of introduction to and expression in an in vitro cell culture. Usually, the DNA constructs will be suitable for replication in a unicellular host, such as yeast or bacteria i.e. negative bacteria E.coli. but may also be intended for introduction and integration within the genome of cultured mammalian or other eukaryotic cell lines. DNA constructs prepared for introduction into bacteria or yeast will include a replication system recognized by the host. Available expression vectors, which include the replication system and transcriptional and translational regulatory sequences together with an insertion site for the N-myc DNA sequence may be employed. (see col. 4,lines 62-68; col. 5, lines 1-15; col. 9, lines 65-66). The polypeptide can be an antibody or antibody fragment. The step of selecting a host cell that expresses the desired polypeptides comprises the steps of contacting said antibody or antibody-fragment-expressing cells with a selected antigen; and identifying a host cell that binds to said selected antigen (see col. 9, line 23-col. 10, line 14). The antigen/polypeptide is labeled with a fluorescers, chemiluminescers, magnetic particles etc. (see col. 6, lines 58-68). The natural or synthetic DNA fragments coding for a desired N-myc fragment will be

incorporated into DNA constructs capable of introduction and expression in cell culture. DNA constructs are suitable for replication in unicellular host such as yeast or bacteria, but may be used with mammalian or other eukaryotic cell lines. (see col. 4, line 63-col. 4, line 1). The vector library is obtained by administering to an animal such as a mouse a desired antigen. The mouse is then killed, the spleen removed, and the spleen cells immortalized. DNA segments that encode distinct antibodies or antibody fragments were obtained and incorporated into a plurality of expression vectors, the vectors expressing antibodies or antibody fragments on the outer membrane surface of a Gram negative host cell, E. coli. (see col. 4, lines 62-68; col. 5, line 1-68). Selected cells that express a desired antibody are subjected to cleavage to release the selected antibody or antibody fragment from the surface of the outer membrane. (see col. 7, lines 27-50).

It would have been obvious to one of ordinary skills in the art to use the general method of obtaining a vector library of Slamon to obtain a vector library for use in the method of Higuchi since both teach using vectors to express desired antibodies/fragments in host cells to the advantage that immortalized cell lines are capable of producing antibodies having a desired specificity. It is advantageous to use monoclonal antibodies because they are highly specific.

Since Higuchi teaches the antibodies expressed in host cell of their invention are secretory type or membrane-bound type and Slamon teaches releasing the selected antibody from the surface of the outer membrane, it would have been obvious to one of ordinary skills in the art to use cleave the secretory type antibodies of Higuchi in order to detect these secretory antibodies effectively and it is advantageous to cleave these

secretory antibodies from cell membrane to distinguish from the membrane-bound antibodies.

It would also have been obvious to one of ordinary skills in the art to use magnetic beads coupled to antigen as taught by Slamon for detecting antibodies expressed in host cells as taught by Higuchi since Slamon teaches that magnetic beads are capable of coupling to antigen and usable as labels for detecting antibodies. Magnetic beads advantageous as carriers or labels for separation and detection of antibodies in general. It is also well known that manipulation of magnetic particles require a magnetic field.

Response to Arguments

Applicant's arguments with respect to claims 1-3, 6-12, 15-26, 46 have been considered but are moot in view of the new ground(s) of rejection.

Allowable Subject Matter

Claims 9, 10, 12, 22-24 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Pensee T. Do
Patent Examiner
October 3, 2006

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